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RADIATION EXPOSURE AND CENTRAL NERVOUS SYSTEM CANCERS: A CASE-CONTROL STUDY AMONG WORKERS AT TWO NUCLEAR FACILITIES

Arvind V. Carpenter
W. Dana Flanders
Edward L. Frome
Douglas J. Crawford-Brown
Shirley A. Fry

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RADIATION EXPOSURE AND CENTRAL NERVOUS SYSTEM CANCERS: A CASE-CONTROL STUDY AMONG WORKERS AT TWO NUCLEAR FACILITIES

Arvind V. Carpenter, D.D.S., Dr.P.H.
Center for Epidemiologic Research
Medical and Health Sciences Division

Oak Ridge Associated Universities, Oak Ridge, Tennessee

ORAU--282

DE87 007922

W. Dana Flanders, M.D., D.Sc.
Department of Epidemiology, School of Public Health
University of Alabama at Birmingham, Birmingham, Alabama
Current Address: Centers for Disease Control, Atlanta, Georgia

Edward L. Frome, Ph.D.
Mathematics and Statistics Research
Engineering Physics and Mathematics Division
Oak Ridge National Laboratory, Oak Ridge, Tennessee

Douglas J. Crawford-Brown, Ph.D.
Department of Environmental Sciences and Engineering
University of North Carolina, Chapel Hill, North Carolina

Shirley A. Fry, M.D., M.P.H.
Center for Epidemiologic Research
Medical and Health Sciences Division
Oak Ridge Associated Universities, Oak Ridge, Tennessee

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This study concerns work undertaken as part of the Health and Mortality Study of Department of Energy (DOE) workers being conducted by Oak Ridge Associated Universities (ORAU) with the collaboration of the Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, and Departments of Epidemiology and Environmental Sciences and Engineering, School of Public Health, University of North Carolina at Chapel Hill under contract number DE-AC05-76OR00033 between the DOE Office of Energy Research and ORAU. Part of the data used was collected under a previous contract with the Atomic Energy Commission and later with the U.S. Energy Research and Development Administration (No. E11-1-3428) under the direction of Dr. T. F. Mancuso, University of Pittsburgh.

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THE HISTORY OF THE UNITED STATES

CHAPTER I. THE DISCOVERY OF AMERICA.

IN THE YEAR 1492, CHRISTOPHER COLUMBUS, an Italian navigator, discovered the continent of America.

He sailed from Spain in the month of August, and after a long and dangerous voyage, he reached the coast of America on the 12th of October.

He was the first European who discovered the continent, and his discovery opened a new world to the eyes of the whole world.

From that time, the continent of America has been the scene of many great events, and has become one of the most powerful nations of the world.

It has been the seat of many wars, and has seen the rise and fall of many empires.

It has been the home of many great men, and has produced many of the most famous names in the history of the world.

It has been the theatre of many great events, and has seen the birth of a new nation.

It has been the scene of many great battles, and has seen the fall of many great empires.

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ABSTRACT

A nested case-control study was conducted among workers employed between 1943 and 1977 at two nuclear facilities to investigate the possible association of primary malignant neoplasms of the central nervous system (CNS) with occupational exposure to ionizing radiation from external and internal sources. Eighty-nine white male and female workers, who according to the information on death certificates died of primary CNS cancers, were identified as cases. Four matched controls were selected for each case.

External radiation exposure data were available from film badge readings for individual workers, whereas radiation dose to lung from internally deposited radionuclides, mainly uranium, was estimated from area and personnel monitoring data and was used in analyses in lieu of the dose to the brain. Matched sets were included in the analyses only if information was available for the case and at least one of the corresponding controls. Thus, the analyses of external radiation included 27 cases and 90 matched controls, and 47 cases and 120 matched controls were analyzed for the effects of radiation from internally deposited uranium.

No association was observed between deaths from CNS cancers and occupational exposure to ionizing radiation from external or internal sources. However, due to the small number of monitored subjects and low doses, a weak association could not be ruled out.

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INTRODUCTION

Primary malignant tumors of the brain and other parts of the central nervous system (CNS) constitute only about 2 percent of all cancers in humans, although these tumors are the tenth most common cause of cancer deaths among males and twelfth among females (Cutler and Young 1975). The age-adjusted incidence rate of primary cancers of CNS in all areas included in the SEER program, during 1978-1981, was highest among white males (7.1/100,000) and lowest in nonwhite females (3.0/100,000). The incidence rate in white females was 5.0 per 100,000 and for nonwhite males was 4.4 per 100,000 population (Horn et al. 1984). Since CNS cancers are relatively common in childhood and during the productive years of life, they are the fourth leading cancer cause of loss of work years among males and eighth among females (Murray and Axtell 1974). During the period 1960-1973, the observed median survival time for CNS cancers was 0.8 year for white patients and 0.7 year for black patients (Axtell, Asire, and Myers 1976).

Despite the relatively high morbidity and mortality rates associated with CNS cancers, little is known about possible risk factors. Occupational exposures may be etiologically important since increased rates have been reported among several industrial populations (Thomas and Waxweiler 1986). A few epidemiologic studies have reported that persons employed in the nuclear industry may be at increased risk of developing CNS cancers (Polednak 1980; Johnson 1980; Voelz et al. 1983; Hadjimichael et al. 1983; Acquavella et al. 1985), although no increased risk was found

in other studies (Mancuso, Stewart, and Kneale 1977; Gilbert and Marks 1979; Polednak and Frome 1981; Beral et al. 1985; Checkoway et al. 1985).

The possibility that the increased risk might be due to radiation exposure, a suspect CNS carcinogen (Modan et al. 1974; Shore, Albert, and Pasternack 1976; Darby, Nakashima, and Kato 1985), was investigated by Reyes and colleagues (1984). They conducted a case-control study of CNS tumors among a cohort of nuclear workers in which an apparent excess of CNS cancers had occurred, but failed to find an association of risk with external or internal radiation.

Our epidemiologic investigation was a nested case-control study of workers employed at two nuclear facilities located in Oak Ridge, Tennessee (the Y-12 Plant and Oak Ridge National Laboratory). Cases and controls in this study were selected from white male and female workers hired between 1943 and 1977 at these facilities. Workers at the Y-12 Plant (the Y-12 cohort) under the management of the Tennessee Eastman Corporation from 1943 to 1947 were involved in the enrichment of uranium-235 in the form of uranium tetrachloride via an electromagnetic separation process and the subsequent conversion to uranium tetrafluoride (Polednak and Frome 1981). Since 1947 the Y-12 Plant has been operated by the Union Carbide Corporation, and the workers have been involved primarily in fabrication and certification of components for nuclear weapons (Polednak 1980). Workers at Oak Ridge National Laboratory (the ORNL cohort) have been involved in research and the development of technology for production of energy (Checkoway et al. 1985).

Several preliminary studies have assessed CNS cancer mortality among these cohorts. In a study of Y-12 Plant workers involved in uranium

conversion and enrichment between 1943 and 1947, the standardized mortality ratio (SMR) for CNS cancers was 95 (observed deaths = 32) (Polednak and Frome 1981). A preliminary analysis of mortality among a cohort of white males employed at the Y-12 Plant after 1947 (nuclear weapons plant) showed an SMR of 197 (95 percent confidence interval [CI] = 80-400, observed deaths = 7) for CNS cancers (Polednak 1980). An analysis of workers at ORNL by Checkoway et al. (1985) showed a CNS cancer SMR of 96 (observed deaths = 9) when compared to the U. S. population.

The present study was motivated in part by the finding of more than the expected number of CNS cancer deaths among the workers employed at the Y-12 Plant after 1947 (Polednak 1980). The primary purpose of the study was to investigate the association, if any, of CNS cancers among these workers with occupational exposure to ionizing radiation from external and internal sources.

These workers were followed to determine the vital status by periodic requests for information to the Social Security Administration (SSA), state Motor Vehicle Divisions, the Veterans Administration, and the Civil Service Retirement System (details are presented in Appendix A).

METHODS

Cases and Matched Controls

Cases consisted of all white male and female workers in the two facilities who, according to the information on death certificates (underlying cause of death), died of primary malignant neoplasms of the brain or other parts of the CNS (USDHEW 1968, International Classification of Diseases, Adapted for the United States, Eighth revision [ICDA8] codes 191 and 192) between 1943 and 1979 (see Appendix B). Eighty-nine cases were identified (Table 1). Fourteen of these cases died from a CNS cancer of unspecified site but of known histologic type (ICDA8 - 192.9).

Information about the cancer site in these fourteen cases was requested from hospitals at which these subjects were treated or died. All of the eleven responses indicated that the subjects had died from brain cancer, thus permitting nosological reclassification (as ICDA8 - 191) (Carpenter 1986).

For each case, four controls were selected who matched the case on sex, cohort (Y-12 or ORNL), year of birth, and year of hire. Controls may have been alive or deceased at the study cutoff date but must have lived as long as the matching case; however, their exposure was considered only up to the date the corresponding case died. If more than four subjects were identified who matched a case on each matching factor, then four were selected at random using a computer algorithm. When fewer than four matching controls could be identified, the matching criteria were gradually relaxed until four or more potential controls were found. The

TABLE 1. BRAIN AND OTHER CNS CANCER CASES, BY COHORT, SEX, AND SITE

Site	Y-12		ORNL		Multi ^a		Total	
	WM	WF	WM	WF	WM	WF	WM	WF
Brain	51	15	10	0	6	0	67	15
Other CNS	5	2	0	0	0	0	5	2
	—	—	—	—	—	—	—	—
Total	56	17	10	0	6	0	72	17

^a Worked in both cohorts under study during 1943-1977

WM- White males

WF- White females

matching criteria were relaxed to obtain controls for seven cases.

Additional details are presented in Appendix B.

Data Collection

Demographic and Employment Information

Information on demographic variables, such as race, sex, birth date, date of death (if dead), and cause of death (coded to the eighth revision of the ICDA code) was available at Oak Ridge Associated Universities, Center for Epidemiologic Research, in the computerized data base of the Health and Mortality Study of U. S. Department of Energy Workers (Lushbaugh 1982). For all workers, work histories, including cohort,

dates of hire and termination, departments, job titles, and pay code (a surrogate for socioeconomic status), had been abstracted previously, primarily from personnel files (payroll records and summary earning cards) and employment history forms (Mancuso, Sanders, and Brodsky 1964-1977). Each job title was assigned a "job classification" code as professional, skilled, or unskilled (PSU), based on the assumption of educational requirement for the job (McClanahan 1986). The PSU code was used, in addition to the pay code (hourly or monthly), as a surrogate measure of socioeconomic status.

External Radiation

The Y-12 Plant. Workers at the Y-12 Plant, under the management of the Tennessee Eastman Corporation from 1943 to 1947, were involved in the enrichment of uranium-235 in the form of uranium tetrachloride via an electromagnetic process and the subsequent conversion to uranium tetrafluoride. Since the process involved manual work, these workers were potentially at risk of exposure to varying amounts of ^{238}U and ^{235}U . These radionuclides, and most of their daughter products, emit mainly alpha radiation, which does not penetrate the skin, so irradiation from external sources was not a major hazard. The major radiation hazard during this period was from inhaled uranium. Methods for measuring external and internal radiation either were not available or were in their developmental stages during this period of the plant's operations (Cookfair 1982). Because no external radiation monitoring program was available at Y-12 until 1948, all workers employed between 1943 and 1947

were excluded from the analyses for which external radiation data were required.

In May 1947, the Union Carbide Corporation (UCC) assumed management of the Y-12 Plant for the Atomic Energy Commission, and since then workers have been involved in nuclear weapons fabrication, nuclear fuel reprocessing, and the processing of many radioactive materials, including uranium, thorium, and plutonium. The potential for exposure to radiation from both external and internally deposited sources has been present at the plant during all years of operation. The film badge program to monitor external radiation was established in 1948; from the beginning of monitoring until 1961, only those employees with an exposure potential greater than 10 percent of the then-current radiation protection standard, which then was 15 rem per year, were monitored for exposure to external radiation--mainly gamma radiation. In 1962, a film dosimeter was integrated into the identification badge that every employee had to wear (West 1984). In all, about 70 percent of workers employed after 1947 at the Y-12 Plant were monitored for external radiation (at some time during their employment) (Strom 1983).

The frequencies with which film badges were read depended on the worker's potential for exposure to external radiation and on the health physics practices at the time. Hence, some workers had their film badges read four times a year, while most had them read only once a year (West 1984). The reported radiation doses were based on the dose delivered to the film badge, the location of which may have varied. Doses to specific organs in the body may differ from this external radiation dose measurement. In general, it is valid to assume that film badge readings

are proportional to total body doses and that a selective bias would not be introduced because these readings were used in the analyses for both cases and controls in the same fashion. The average cumulative lifetime dose for monitored workers at the Y-12 Plant was about 1 rem (Strom 1983).

Oak Ridge National Laboratory (ORNL). Oak Ridge National Laboratory has been involved in research and development of energy alternatives. Initially, it served as a pilot plant for the Hanford facility, and a small quantity of plutonium was produced at ORNL.

Monitoring of external radiation, primarily gamma rays, has been conducted since 1943. Personnel monitoring devices used at ORNL to register exposure to radiation from external sources include pocket ionization chambers (February 1943-May 1944), film badge dosimeters (June 1944-December 1975), and since 1975, thermoluminescent dosimeters (Parrish 1983; Muir 1984). Before 1950, only workers considered at risk by the health physics staff of being exposed to external radiation were required to wear a film badge; since 1951 film badge monitoring has been routine for all workers. In 1959, a film dosimeter integrated in the identification badge was provided to all employees.

From 1944 to 1956 film badges were evaluated weekly; thereafter, the monitoring periods were quarterly for workers who were likely to exceed 10 percent of the annual dose limits (the maximum permissible dose to critical organs was 0.3 rem/week or 15 rem in a year). For others, film badges were processed annually. In all, about 85 percent of workers at ORNL were monitored at some time during their employment period for exposure to external radiation. About 88 percent of monitored workers each had a cumulative lifetime dose equal to or less than 1 rem (Parrish 1983).

Internal Radiation

The Y-12 Plant. Uranium--at various levels of enrichment--was the major source of internal radiation exposure in the Y-12 Plant under the management of the Tennessee Eastman Corporation from 1943 to 1947. At that time, personal monitoring techniques were in the developmental stage; hence, few people had uranium urinalyses performed, and whole-body counting was nonexistent. Thus, for the workers at the Y-12 Plant during 1943-1947, the internal radiation exposure information came primarily from limited air monitoring samples collected in some of the uranium processing departments. Air monitoring data were grouped by location; the data included information on types of processes carried out at each location. An average value of the air monitoring samples was used to calculate the lung dose. Few individuals had uranium urinalyses performed; hence, the air monitoring information was used in this study.

The available information included (Cookfair 1982; Beck et al. 1983)

1. uranium air concentrations by building/department/room
2. chemical and physical forms and isotopic ratios for various uranium compounds by building/department/room
3. processes carried out in building/department/room
4. job title descriptions by building/department/room
5. days worked by employees by job title/department.

To utilize these data, certain assumptions were made: (1) workers did not use respirators, (2) the uranium concentrations measured by the

air samples in working areas were representative of uranium concentrations in the air breathed by workers, and (3) each worker had a similar metabolism and respiration rate of 9.6 m^3 (men) per eight-hour work shift or 9.12 m^3 (women) per eight-hour work shift. Industrial hygiene reports and other records suggest that the first assumption is fairly accurate, although some uncertainty may have been introduced into dose calculations because of the second and third assumptions. The concentration of uranium dust present in the air breathed by a worker may have been different from that in the location of the air sampling device, and individuals do differ as to metabolism and respiration rates (Cookfair 1982).

A dose in rem delivered to the brain could not be estimated from the available data or in the absence of brain dosimetry models. The solubility of uranium compounds may affect the dose to brain because the insoluble compounds may remain in the lung, whereas soluble compounds may travel to different parts of the body via the circulatory system. Since the main hazard at the Y-12 Plant was from insoluble uranium compounds, the lung dose may be related monotonically to the dose to the brain. Thus, proportionality was assumed between the radiation dose to the lung and brain, and the lung dose, estimated using the existing models, was used as a surrogate measure. The annual lung dose was estimated, for workers in monitored departments, as described in Appendix C. The procedure took into account the particle size, level of enrichment, and the solubility of the uranium compounds. The annual lung dose estimates were summed to obtain an estimate of the cumulative lung dose up to the year of death of the case for each member of the matched set. The workers

in monitored departments were divided into four exposure groups based on the cumulative estimated lung doses:

Group 1 -- ≤ 15 rem

Group 2 -- > 15 & ≤ 30 rem

Group 3 -- > 30 & ≤ 45 rem

Group 4 -- > 45 rem

Since air monitoring data were not available for every department, these workers were divided into three categories:

Category 1 -- always worked in monitored departments

Category 2 -- always worked in nonmonitored departments

Category 3 -- worked in both monitored and nonmonitored departments

Some of the nonmonitored departments (e.g., accounting, payroll, etc.) were not involved in uranium processing. Workers in these departments were considered as not exposed to uranium dust. For workers in the remaining nonmonitored departments, the possibility existed for occasional exposures to low and high levels of uranium. Thus, where no air monitoring data were available for a department, workers were assigned to one of three exposure ranks for that portion of his/her dose assessment (Cookfair 1982; Beck et al. 1983):

Rank 1 - exposure unlikely (e.g., accountants, clerical staff)

Rank 2 - occasional exposure to low levels possible (e.g., guards, janitors)

Rank 3 - occasional exposure to high levels possible (e.g., electricians, maintenance workers)

Lung doses were estimated for all workers in category 1 (always worked in monitored departments), and these workers were included in the analyses for internal radiation exposure. Category 2 workers (always worked in nonmonitored departments), who worked exclusively in departments assigned rank 1, were considered to be unexposed and were included in group 1 (≤ 15 rem) in the analyses, whereas workers with rank 2 or 3 were not included in the analyses. We can be reasonably certain that workers with rank 1 were unexposed, but the classification of workers with rank 2 or 3 according to the dose groups was not feasible. Workers in category 3 (worked in both monitored and nonmonitored departments) had a lung dose from the monitored part of their work history and a rank(s) for employment in nonmonitored department(s). Workers who had rank 1 for all nonmonitored jobs were included in the analyses, classified according to the lung dose from the monitored part of the employment; for example, a worker who has a dose of 25 rem from the employment in the monitored departments and rank 1 for all nonmonitored jobs was classified in group 2 (> 15 and ≤ 30 rem). Few of the category 3 workers had more than 45 rem cumulative lung dose from the monitored part of their work history; they were included in group 4 (> 45 rem) regardless of the rank(s) for the nonmonitored part of the employment. All other workers in category 3 were excluded from the analyses for internal radiation.

For workers employed after 1947 at the Y-12 Plant (under the management of the Union Carbide Corporation), internally deposited uranium was the major source of internal radiation exposure, and there was little potential for internal exposure to other radionuclides. A routine uranium urinalysis program was started in 1950 for workers in the enriched uranium operating departments. The program subsequently was expanded to include most employees who spent 25 percent of their time working with uranium or in uranium areas. In the early 1960s, whole-body counting by in-vivo gamma spectrometry became the primary procedure for monitoring exposure to internally deposited uranium (Strom 1983; West 1984). The spectrometer could measure radioactivity in the chest, and spectrometry was considered a better monitoring technique than urinalysis because at the Y-12 Plant insoluble uranium in the lung has been the major potential radiation hazard. Since 1964, the whole-body counting program has been the principal method of estimating exposure to internally deposited radionuclides (West 1984), and the frequency of participation in the program is based on the exposure potential for the individual worker as determined by the department supervisor and the health physics personnel.

Personnel from departments that had experienced favorable results on both urinalyses and whole-body count programs for a period of five years or more were removed from the routine urinalysis program, after which a small number of employees in these departments were chosen at random for annual evaluation by urinalysis (Strom 1983; West 1984). Uranium urinalyses, however, have continued to be used for evaluation of exposures to the soluble forms of uranium. About 35 percent of the Y-12 cohort was monitored, at some time during their employment, for internal exposure to

radioactive materials. The procedure used to estimate a dose to lung in rem from urinalyses and whole-body counts was previously reported (Strom 1983).

In the absence of appropriate metabolic models it was not feasible to estimate the dose to brain, thus, lung dose was used as a surrogate. For each member of a matched set, estimated annual lung doses were accumulated up to the year of death of the case. Workers with an estimated lung dose were classified in four groups based on the cumulative doses: (1) ≤ 15 rem, (2) > 15 and ≤ 30 rem, (3) > 30 and ≤ 45 rem, and (4) > 45 rem. Non-monitored workers were excluded from the analyses.

Oak Ridge National Laboratory (ORNL). Since ORNL always has been a multiprogram research institution, there has been a potential for its workers to be exposed to many radionuclides in small quantities, including plutonium, uranium, tritium, cesium, strontium, and radium. The urinalyses program began in 1951 and the whole-body counting program started in 1962 for individual monitoring of exposure to radiation from internally deposited radionuclides (Mani 1983; Muir 1984).

Since only persons suspected of being at risk were monitored for internally deposited radionuclides, only about 32 percent of the cohort was monitored at some time during employment. In the computerized data files, the results of the urinalyses were recorded in disintegrations per minute (dpm) in a 24-hour period, and the results of whole-body counts were recorded as a fraction (in range, i.e., $< 15\%$, $15-24\%$, $25-49\%$, etc.) of the maximum permissible critical organ burden (MPOB).

For most of the monitored workers, the radionuclides to which they were exposed were not identified (Mani 1983). Therefore, from the

computerized monitoring data; calculation of the lung doses contributed by individual radionuclides was not possible. For this reason, the ORNL workers were not included in the analyses for radiation from internally deposited radionuclides.

However, the exposure to radiation from internal sources was considered to be low at ORNL. None of the monitored workers at ORNL included in this study exceeded one-third of the MPOB.

Analyses

Matched conditional logistic regression analyses for categorical and continuous exposure variables were conducted using a SAS program (PHGLM) (Harrell 1983) and interpreted as described by Breslow and Day (1980). Confidence intervals calculated are approximate because the number of discordant matched sets is generally small. When appropriate, trend tests for dose-response effects were performed (Mantel 1963).

To allow for a five-year or a ten-year latency period, analyses were conducted by excluding the exposures five or ten years prior to the death of each case, respectively, for cases and their matched controls (Rothman 1981). Analyses were also conducted using the modified serially additive expected dose (SAED) method to test the null hypotheses of no association between radiation exposure and occurrence of CNS cancers (Lubin 1983). Analyses were repeated for brain cancer only (ICD8 = 191) and for brain cancers of glial origin.

External Radiation

Workers who were monitored for external radiation at some time during their employment were included in the analyses. However, a matched set (i.e., a case and its matched controls) was included in the analyses only if the case and at least one of the corresponding controls were monitored. Thus, the analyses of external radiation data were restricted to 27 cases and 90 controls from the Y-12 and ORNL cohorts (Figure 1). Only the doses due to penetrating radiation (i.e., gamma, X-ray, proton, and neutron doses) were used in the analyses. Since most of the penetrating external radiation was from gamma rays in both cohorts, simultaneous analysis of the Y-12 and ORNL cohorts should be acceptable (Crawford-Brown 1984). For each of these 117 subjects, periodic film badge readings were summed over each calendar year to calculate his/her annual external radiation dose. For each member of a matched set, annual doses were then summed to calculate a cumulative dose up to the year of death of the case. Also, cumulative doses allowing for five-year and ten-year latency periods were calculated for cases and their matched controls. Average annual dose was calculated by dividing the cumulative dose by duration of employment for each worker included in the analyses.

Internal Radiation

A matched set was included in the analyses only if the case and at least one of the matched controls had estimated lung doses; 47 cases and 120 controls from the Y-12 cohort met this criterion and were included in

FIGURE 1. DESCRIPTION OF WORKERS INCLUDED IN THE ANALYSES OF EXTERNAL RADIATION EXPOSURE

the analyses based on lung doses (Table 2). Estimation of the annual lung doses of the study subjects was done without knowledge of the case-control status of the study subjects. For each member of a matched set, annual lung dose estimates were then summed to provide a cumulative dose up to the year of death of the case. Also, cumulative doses allowing for five-year and ten-year latency periods were determined for cases and their matched controls. Average annual dose was calculated by dividing the cumulative lung dose by duration of employment.

TABLE 2. DESCRIPTION OF CASES AND CONTROLS INCLUDED IN THE ANALYSES FOR INTERNAL RADIATION EXPOSURE

Group	Cases	Controls	Total
Number of workers included in analyses for internal radiation	47	120	167
Y-12 workers (1943-1947)	37	94	131
Worked in monitored area only	20	42	62
Worked in nonmonitored area only (Rank = 1)	11	39	50
Worked in monitored & nonmonitored areas			
lung dose + rank = 1	4	9	13
lung dose > 45 rem	2	4	6
Y-12 workers (after 1947)			
monitored workers	10	26	36

Since only eight matched sets were monitored for radiation exposure from both external and internal sources, analyses to study their joint effects were not conducted.

RESULTS

General Characteristics of Cases and Controls

Distributions of 89 cases of CNS cancers and their 356 controls are presented in Appendix D, Tables D-1 to D-5. The mean and median ages at death for the cases were about 52 years. Eighty-two (92%) of the cases had cancers of brain while the other seven died from cancers of other parts of the CNS. Fifty-six (68%) of these 82 brain cancer cases were known to have had malignant tumors of glial origin, of which 21 (33%) were glioblastomas and 20 (32%) were astrocytomas. No appreciable difference was observed between the mean ages at termination of employment of the cases and controls.

External Radiation

For workers monitored for external radiation (27 cases and 90 controls), demographic characteristics and other distributions are presented in Appendix E, Tables E-1 to E-7. All cases who were monitored for external radiation died of primary malignant brain tumors (ICDA8 code - 191). The cases left employment at later ages and worked longer than the controls. The proportion of hourly paid to salaried workers was similar among cases and controls.

The mean cumulative external radiation (total body penetrating) doses for the cases and the controls were 1.09 rem and 1.22 rem, respectively, with a median of 0.89 rem for the cases and 0.35 rem for the controls

(Table 3). This pattern of exposure (lower mean and higher median among cases than among controls) was similar in the Y-12 and ORNL cohorts (Appendix E, Table E-4).

TABLE 3. DISTRIBUTION OF CASES AND CONTROLS MONITORED FOR EXTERNAL RADIATION BY CUMULATIVE EXTERNAL RADIATION DOSE (percent of cases and of controls in parentheses)

Level	Cases		Controls	
	No. (%)	Mean Duration of Employment (years)	NO. (%)	Mean Duration of Employment (years)
Number of Workers in this Group	27 (100.0)	14.0	90 (100.0)	11.1
<1 rem	16 (59.2)	12.0	68 (75.5)	9.2
≥ 1 & < 2	8 (29.6)	18.8	7 (7.8)	20.8
≥ 2 & < 3	1 (3.7)	14.3	6 (6.7)	12.6
≥ 3 & < 4	2 (7.4)	10.5	2 (2.2)	18.1
≥ 4 & < 5	0 (0.0)	0.0	1 (1.1)	9.0
≥ 5 rem	0 (0.0)	0.0	6 (6.7)	18.3
Mean	1.09 rem		1.22 rem	
Median	0.89 rem		0.35 rem	

Cumulative Dose

Analyses of the cumulative doses of external radiation were not very informative because no case and only 6 controls accumulated any appreciable dose, that is, 5 rem or more (Table 3). The odds ratio, comparing the risk of CNS cancers among workers with 5 or more rem with that among workers with less than 5 rem of external radiation, was 0.0 with a 95 percent confidence interval (CI) from 0.0 to 2.3.

Because of the low doses and small number of subjects, further analyses may contain little meaningful information. For completeness, however, additional analyses were conducted. In one analysis, the cumulative dose was categorized in three groups. Using group I (≤ 1 rem) as the reference category, the odds ratios for group II (1.01-2.0 rem) and group III (> 2 rem) were 5.6 (95% CI = 1.6-19.8, cases = 8) and 0.93 (95% CI = 0.2-4.2, cases = 3), respectively. The trend test was not statistically significant ($p = 0.445$). Results of other categorical analyses for monitored workers are presented in Tables 4 and 5. In a supplemental analysis, results were similar when nonmonitored workers were included in the reference category.

Using the modified SAED method (Lubin 1983), the cumulative external radiation dose for each case was compared to the expected dose estimated from the corresponding matched set. For about half the cases, the observed dose was less than the expected dose ($p = 0.8$), consistent with no association between cumulative external radiation dose and occurrence of CNS cancers (Table 6).

TABLE 4. MATCHED ANALYSES FOR CUMULATIVE EXTERNAL RADIATION DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases
≤ 1 rem	1.00	-----	16
> 1 & ≤ 2	5.20	1.5, 18.3	8
> 2 & ≤ 3	0.99	0.1, 9.6	1
> 3 & ≤ 4	2.20	0.3, 17.2	2
> 4 & ≤ 5	0.00	0.0,	0
> 5 rem	0.00	0.0,	0
Trend test: $p = 0.83$			

TABLE 5. MATCHED ANALYSES FOR CUMULATIVE EXTERNAL RADIATION DOSE BY COHORT

Cohort	Level	Odds Ratio	95% Confidence Interval	No. of Cases
Y-12	≤ 1 rem	1.00	-----	10
	> 1 & ≤ 2	2.64	0.34, 20.6	2
	> 2 rem	0.44	0.04, 4.8	1
ORNL	≤ 1 rem	1.00	-----	4
	> 1 & ≤ 2	12.10	1.28, 115.2	4
	> 2 rem	0.71	0.06, 8.8	1

Trend test for Y-12: $p = 0.74$; for ORNL: $p = 0.63$

TABLE 6. CUMULATIVE EXTERNAL RADIATION DOSE (MILLIREM) FOR CASES AND CONTROLS BY MATCHED SETS

Set	Case [1]	Control 1	Control 2	Control 3	Control 4	Mean for the Set [2]	Difference of [1] & [2]
1	932	675	---	---	---	804	128
2	477	3410	13166	145	158	3471	- 2994
3	3700	668	5106	---	---	3158	542
4	186	1034	207	116	---	386	- 200
5	0	0	0	0	0	0	0
6	304	0	0	0	---	76	228
7	891	438	657	---	---	662	229
8	632	113	806	1437	142	626	6
9	1415	786	0	57	581	568	847
10	1517	1389	2168	7288	720	1976	- 459
11	804	754	3848	---	---	1802	- 998
12	580	580	708	877	918	733	- 153
13	875	407	395	336	369	477	398
14	1070	95	0	835	6850	1770	- 700
15	1195	100	15030	1270	0	3519	- 2324

TABLE 6. CUMULATIVE EXTERNAL RADIATION DOSE (MILLIREM) FOR CASES AND CONTROLS BY MATCHED SETS (continued)

Set	Case [1]	Control 1	Control 2	Control 3	Control 4	Mean for the Set [2]	Difference of [1] & [2]
16	940	2145	60	0	7845	2198	- 1258
17	90	2120	0	1860	20	818	- 728
18	1115	2425	585	315	---	357	758
19	3770	0	2175	2335	300	1716	2054
20	110	20	90	610	30	172	- 62
21	1140	2425	585	315	---	1116	24
22	280	0	55	0	185	104	176
23	2284	1006	0	161	---	863	1421
24	705	18	---	---	---	362	343
25	173	883	577	155	200	398	- 225
26	1725	50	836	0	---	653	1072
27	1690	4670	907	1369	---	2159	- 469
Total	28600					30944	- 2344
Mean	1059					1146	- 87

A matched logistic analysis treating cumulative external radiation dose as a continuous variable was conducted (Table 7). Based on a linear or a quadratic model, the estimated odds ratio decreased as the dose increased, never exceeding unity, although these models fit poorly (Tables 7 and 8). With a linear-quadratic model, which was a better fit, the odds ratio peaked at 2 rem of cumulative external radiation and then decreased and was less than unity for exposures of 5 rem or more (Table 8).

Average Annual Dose

Average annual external radiation dose, calculated by dividing the cumulative dose by duration of employment, was categorized into group I--average yearly occupational dose ≤ 180 millirem, group II--average yearly dose 181-360 millirem, and group III--average yearly dose > 360 millirem. These arbitrary limits were chosen in part because radiation dose from natural background radiation and medical procedures averages about 180 millirem per year (Chanlett 1973; BEIR III 1980; Shleien and Terpilak 1984). Most of the cases and controls were in group I (Table 9). The matched odds ratio for group II was 0.63 (95% CI = 0.05-7.5) and for group III was 0.94 (95% CI = 0.14-6.34) when compared to group I. The trend test was statistically not significant ($p = 0.85$). When groups II and III were combined and compared to group I the odds ratio was 0.8 (95% CI = 0.17-3.7).

TABLE 7. RESULTS OF FITTING DIFFERENT CONDITIONAL LOGISTIC REGRESSION MODELS TO THE MATCHED SETS MONITORED FOR EXTERNAL RADIATION

Model	No. of Parameters	-2 Log Likelihood Ratio	Chi-Square	$\beta_1 \pm$ Standard Error	
				EXT	EXT ²
1	0	77.50	---	---	---
2	1	77.40	0.10	- 0.04 $\pm$ 0.12	
3	1	76.12	1.38		- 0.02 $\pm$ 0.03
4	2	65.82	11.68	2.0.7 $\pm$ 0.78	- 0.46 $\pm$ 0.21

EXT = Cumulative External Radiation Dose

EXT² = Cumulative External Radiation Dose²Model # 2: OR = exp (β_1 EXT)Model # 3: OR = exp (β_2 EXT²)Model # 4: OR = exp (β_1 EXT + β_2 EXT²)

Chi-square = (-2 log likelihood ratio for Model # 1)

- (-2 log likelihood ratio for the model of interest)

TABLE 8. ODDS RATIOS FOR SPECIFIC DOSES OF EXTERNAL RADIATION CALCULATED FROM REGRESSION MODELS IN TABLE 7

Dose	Linear	Odds Ratio Quadratic	Linear-Quadratic
0 rem	1.00	1.00	1.00
1 rem	0.97	0.98	5.00
2 rem	0.93	0.92	9.97
3 rem	0.90	0.81	7.93
4 rem	0.87	0.69	2.51
5 rem	0.84	0.56	0.32
6 rem	0.81	0.44	0.02

TABLE 9. MATCHED ANALYSES FOR AVERAGE ANNUAL EXTERNAL RADIATION DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases	No. of Controls
≤ 180 millirem	1.0	-----	24	78
> 180 & ≤ 360	0.6	0.05, 7.5	4	5
> 360 millirem	0.9	0.10, 6.3	2	8

Trend test: $p = 0.85$

Maximum Annual Dose

Maximum annual dose for each study subject was also examined; none had exceeded 5 rem in any year, the current annual occupational external radiation protection standard. For completeness, we categorized these workers into three groups:

- I -- received 500 millirem or less each year
- II -- received 501-1000 millirem in any year
- III -- received more than 1000 millirem in any year

The odds ratios for groups II and III were 3.4 (95% CI = 0.7-16.0) and 0.8 (95% CI = 0.1-4.1), respectively, when compared to group I (Table 10).

When groups II and III were combined because of the small numbers, the odds ratio comparing subjects with more than 500 millirem to those with 500 millirem or less was 1.6 (95% CI = 0.5-5.2).

TABLE 10. MATCHED ANALYSES FOR MAXIMUM ANNUAL EXTERNAL RADIATION DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases	No. of Controls
≤ 500 millirem	1.0	-----	21	76
> 500 & ≤ 1000	3.4	0.7, 16.0	4	3
> 1000 millirem	0.8	0.1, 4.1	2	11

Trend test: $p = 0.87$

The matched odds ratio for external radiation was not confounded by any of 26 chemicals for which we had information, socioeconomic status, or duration of employment. These analyses were repeated allowing for five-year and ten-year latency periods, with similar results. The results were also similar when cancers of glial cell origin were analyzed separately.

Internal Radiation

Demographic and other characteristics for the 47 cases and 120 controls included in the analyses of lung doses from internally deposited uranium are presented in Appendix F, Tables F-1 to F-6. The mean cumulative lung dose for the cases and the controls were 18.5 rem and 30.7 rem, respectively, with a median of 3.5 rem for the cases and 0.5 rem for the controls (Table 11).

TABLE 11. MATCHED ANALYSES FOR CUMULATIVE LUNG DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases	No. of Controls
≤ 15 rem	1.0	-----	32	88
> 15 & ≤ 30	2.8	0.65, 11.9	5	6
> 30 & ≤ 45	2.7	0.80, 9.3	5	6
> 45 rem	0.8	0.30, 2.3	5	20
Mean Cumulative Lung Dose			18.5 rem	30.7 rem
Median Cumulative Lung Dose			3.5 rem	0.5 rem
Trend test: $p = 0.87$				

Cumulative Lung Dose

We arbitrarily categorized the workers based on the cumulative lung doses into four groups (Table 11) as follows:

Group 1 -- ≤ 15 rem (reference group)

Group 2 -- > 15 & ≤ 30 rem

Group 3 -- > 30 & ≤ 45 rem

Group 4 -- > 45 rem

The odds ratios for Groups 2, 3, and 4 were 2.77 (95% CI = 0.65-11.9), 2.67 (95% CI = 0.77-9.3), and 0.8 (95% CI = 0.3-2.3), respectively. The trend test lacked statistical significance ($p = 0.87$). Results of other categorical analyses for monitored workers are presented in Table 12. In

a supplemental analysis, nonmonitored workers were included in the reference group, and the matched odds ratios for Groups 2, 3, and 4 became 2.1 (95% CI = 0.8-5.6), 3.4 (95% CI = 1.1-10.6), and 0.8 (95% CI = 0.3-2.1).

TABLE 12. MATCHED ANALYSES FOR CUMULATIVE LUNG DOSE BY COHORT

Cohort	Level	Odds Ratio	95% Confidence Interval	No. of Cases
Y-12 (1943-1947)	≤ 15 rem	1.00	-----	23
	> 15 & ≤ 30	2.97	0.5, 15.9	4
	> 30 & ≤ 45	2.82	0.8, 10.0	5
	> 45 rem	1.03	0.3, 3.1	5
Y-12 (After 1947)	≤ 15 rem	1.00	-----	9
	> 15 & ≤ 30	1.73	0.1, 30.7	1
	> 30 & ≤ 45	0.00	0.0,	0
	> 45 rem	0.00	0.0,	0

Using the modified SAED method (Lubin 1983), the cumulative lung dose for each case was compared to the expected dose estimated from the corresponding matched set. The observed dose was less than the expected dose for more than half of the cases ($p = 0.7$), consistent with no association between cumulative lung dose and occurrence of CNS cancers (Table 13).

TABLE 13. CUMULATIVE LUNG DOSE (MILLIREM) FOR CASES AND CONTROLS BY MATCHED SETS

Set	Case [1]	Control 1	Control 2	Control 3	Control 4	Mean for the Set [2]	Difference of [1] & [2]
1	0	0	0	0	0	0	0
2	0	0	52480	0	----	13120	- 13120
3	154271	0	29872	570951	39318	158882	- 4611
4	32052	0	----	----	----	16026	- 16026
5	0	12768	104	0	----	3218	- 3218
6	0	0	0	----	----	0	- 0
7	474	335	37881	639	----	9832	- 9358
8	10617	54158	236	----	----	21670	- 11053
9	8395	1981	0	----	----	5188	- 3207
10	26092	0	558	0	----	6662	- 19430
11	24318	6801	44891	----	----	25336	- 1018
12	32853	81444	548	0	----	28711	- 4142
13	203	38487	0	3739	----	10607	- 10404
14	0	0	114	----	----	38	- 38
15	24685	0	----	----	----	12342	- 12342
16	48181	0	0	0	60146	21665	- 26516
17	0	0	----	----	----	0	- 0
18	0	62305	309	23	----	15659	- 15659
19	33426	7008	413346	205582	1080	132088	- 98662
20	17531	27366	459989	----	----	168295	- 150764
21	104	91	1376	0	----	392	- 288
22	0	62	316804	----	----	105622	- 105622
23	0	0	0	----	----	0	- 0
24	0	44819	56727	0	4681	21245	- 21245
25	171634	116192	6399	14957	----	77295	- 94339

TABLE 13. CUMULATIVE LUNG DOSE (MILLIREM) FOR CASES AND CONTROLS BY MATCHED SETS
(continued)

Set	Case [1]	Control 1	Control 2	Control 3	Control 4	Mean for the Set [2]	Difference of [1] & [2]
26	60949	4492	0	----	----	21813	39136
27	0	0	----	----	----	0	0
28	972	0	4649	37024	----	10661	- 9689
29	558	0	104017	214	80043	36966	- 36408
30	6399	0	0	----	----	2133	4266
31	40680	139312	1687	118143	0	59964	- 19284
32	5053	15075	19017	0	----	9786	- 4733
33	2880	277	62257	----	----	21804	- 18924
34	642	0	0	----	----	214	428
35	5120	0	0	----	----	1706	3414
36	32697	15131	259	0	----	12021	20676
37	73146	0	----	----	----	36573	36573
38	3550	13300	11699	14785	----	10833	- 7283
39	169	0	0	838	9430	2087	- 1918
40	24177	13595	45089	----	----	27620	- 3443
41	3550	6289	9490	402	776	4101	- 551
42	2867	0	----	----	----	1433	1434
43	0	0	0	0	----	0	0
44	6343	7676	422	----	----	4823	1520
45	13991	8388	59797	15869	305	19670	- 5679
46	0	72710	----	----	----	36355	- 36355
47	0	5078	11119	----	----	5399	- 5399
Total	868609					1180185	- 311247
Mean	18481					25110	- 6629

Average Annual Lung Dose

Average annual lung dose was analyzed after categorizing doses into three groups (Table 14). The majority of cases and controls received less than 1.5 rem. In a matched analysis, the odds ratio for group II (> 1.5 & ≤ 15 rem) compared to group I (≤ 1.5 rem) was 0.7 (95% CI = 0.2-2.2). For group III (> 15 rem), the odds ratio was 1.7 (95% CI = 0.7-4.3). The trend test did not reach statistical significance ($p = 0.35$).

Maximum Annual Lung Dose

In order to evaluate the effect of maximum lung dose, workers were categorized into three groups based on their maximum annual lung doses (Table 15). About 50 percent of workers were in group I (≤ 1.5 rem). The matched odds ratios for group II (> 1.5 & ≤ 15 rem) and group III (> 15 rem) compared to group I were 1.6 (95% CI = 0.6-4.1) and 1.7 (95% CI = 0.7-4.2), respectively. The trend test was not statistically significant ($p = 0.21$).

Results were unchanged when analyses were repeated allowing for five-year and ten-year latency periods. The matched odds ratio for internal radiation was not confounded by any of 26 chemicals, for which we had information, or by socioeconomic status or duration of employment.

TABLE 14. MATCHED ANALYSES FOR AVERAGE ANNUAL LUNG DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases	No. of Controls
≤ 1.5 rem	1.0	-----	26	68
> 1.5 & ≤ 15	0.7	0.2, 2.2	5	19
> 15 rem	1.7	0.7, 4.3	16	33

Trend test: $p = 0.35$

TABLE 15. MATCHED ANALYSES FOR MAXIMUM ANNUAL LUNG DOSE

Level	Odds Ratio	95% Confidence Interval	No. of Cases	No. of Controls
≤ 1.5 rem	1.0	-----	23	68
> 1.5 & ≤ 15	1.6	0.6, 4.1	12	26
> 15 rem	1.7	0.7, 4.2	12	26

Trend test: $p = 0.21$

DISCUSSION

In the analyses of radiation exposure from external and internal sources, we did not observe a dose response, and the odds ratios were less than unity at the highest levels of cumulative exposures. Also, none of the odds ratios from the analyses of the average annual or the maximum annual doses was statistically significantly different from one. The results of this study, therefore, do not support an association between CNS cancers and exposure to either external radiation at the low levels experienced by the study subjects or to radiation exposure from internally deposited uranium. These results are consistent with those of Reyes and colleagues (1984), who failed to detect any association between CNS cancers and exposure to external radiation, to plutonium, or to other occupational risk factors among workers at a nuclear weapons fabrication plant.

However, our ability to study the effects of radiation exposure from external and internal sources was limited. While exposure assessment for external radiation was based on film badge readings and may have been fairly accurate, the number of subjects available for these analyses was small, and the radiation doses generally were low. For example, the average occupational dose from external radiation for the study subjects was lower than that from the background level from natural and man-made sources combined. For internal radiation, the lung dose had to be used as a surrogate for the dose to the brain. Since the lung doses were estimated without knowledge of the case-control status, any associated misclassification should bias the odds ratios towards unity (Copeland et al. 1977).

Further, misclassification and the associated bias towards the null could have occurred because the diagnosis of CNS cancer was confirmed with pathologic reports for only 12 percent of all the cases (Smith 1983). Moreover, confounding factors for which adjustment could not be made, such as occupational exposures prior or subsequent to employment in one of the Oak Ridge facilities, could have distorted the results. The matched study design and matched analyses, however, precluded confounding by several demographic factors including age, sex, cohort, and socioeconomic status. Selection bias, a potentially important source of bias particularly in case-control studies, is probably of less importance in this study than in many other case-control studies because of the nested study design and because of the relatively complete follow-up of the cohorts from which subjects were selected.

Thus, while significant associations were not observed, because of the small number of subjects, low doses, and potential misclassification due to the uncertainties in dose estimates, small effects could remain undetected in a study such as this. Similar conclusions were drawn from separate analyses of cases dying only from brain cancer known to be of glial origin. Increased mortality due to CNS cancers has been observed among workers in industries in which radiation is not a hazard (e.g., petrochemical, oil refineries, vinyl chloride; Thomas and Waxweiler 1986), suggesting that as yet unidentified common etiologic factors, causally related to CNS cancer occurrence, may be present among all these industries or among populations employed in them.

APPENDIX A

VITAL STATUS DETERMINATION

The U. S. Department of Energy Death Certificate Retrieval Office (DCRO) ascertained vital status and provided death information for this study according to the following general procedure.

Vital status was determined initially by the Social Security Administration (SSA) with results reported in five categories:

1. Impossible The Social Security Number (SSN) of the SSN/name pair had not yet been issued by SSA and was not a valid number.
2. Nonmatch The SSN of the SSN/name pair was a valid number but the name did not match the name(s) SSA knew to be associated with that SSN.
3. Unknown The SSN/name pair was valid but there was no current action on the SSA records and the status was uncertain.
4. Assumed Alive The SSN/name pair was valid and the employee was currently paying into or receiving benefits from SSA, or the SSN/name pair did not fall into one of the other vital status categories.
5. Declared Dead The SSN/name pair was valid and the SSA records had an indication of death.

Prepared by Toni Newport, M.P.H., Oak Ridge Associated Universities.

Names of individuals in the "impossible" and "nonmatch" categories were sent to the Center for Epidemiologic Research (CER) error-correction system for resolution. The "unknown" records were sent to other vital status sources (state Divisions of Motor Vehicle, the Veterans Administration, the Civil Service Retirement System, National Death Index) to determine a "dead" or "alive" status. The names of individuals with an "assumed alive" status were returned to SSA periodically until a "dead" status was assigned. The SSA results for the "declared dead" category were reported in three groups:

1. State of Claim Date of death and the state where the death claim was filed.
2. State of Residence Date of death and the state of last residence.
3. Funeral Directors Date of death provided by funeral director's notice. No state was indicated for this group.

Thirty-two state death indexes maintained at CER were searched by DCRO for death certificate records for individuals declared dead by all vital status sources. When an individual was located on an index, a request was made to the appropriate state for a copy of the death certificate. Requests were sent also to the remaining 18 states for death index searches and copies of the death certificates.

When a death certificate was received, the date of death and the demographic data from the certificate were entered into the computerized

death file. A computerized comparison of the demographic data from the death file and the demographic data from the original employee roster was made for each individual. This procedure verified that the death certificate retrieved using vital status sources information was the correct certificate for the individual in the study population. When a certificate could not be verified through the computerized system, additional information (parents' names, birthplaces, etc.) was requested from the CER archival system.

The certificates were coded to the underlying cause of death according to the Eighth Revision of the International Classification of Diseases, Adapted for Use in the United States (USDHEW 1968). If cancer was not the underlying cause but "cancer" appeared on the certificate, it was coded in addition to the underlying cause. Those certificates on which the date of death was later than December 31, 1978, were coded to the ICDA Ninth Revision in addition to the eighth revision code. These codes were then entered into the computerized death file.

APPENDIX B

SELECTION OF SUBJECTS

Cases

Cases consisted of all white male and female workers employed at the two facilities under study who, according to the information on death certificates (underlying cause of death), died of primary malignant neoplasms of brain or other parts of the central nervous system (CNS) (ICDA 8th revision codes 191, 192) between 1943 and 1979. Of 89 identified cases, 14 died from a CNS cancer of unspecified site but of known histologic type (ICDA8 - 192.9). Information about the site of CNS cancer for these workers was requested from the hospital where the subject was treated or died. All eleven responses received indicated that the subject had died from brain cancer, permitting appropriate reclassification (as ICDA8 - 191) for analyses.

Controls

Individuals in the master roster who were employed in one and only one Oak Ridge facility (Y-12 or ORNL) were selected (n = 68,052). From this group, records with race = w (white) and with known birth date were selected (n = 62,426). Eighty-three CNS cancer cases occurred in this group. A dataset was created with the following attributes for these individuals: ID number, sex, race, birth date, survival time, cohort (Y-12 or ORNL), year when first hired, and pay code. Survival time was

calculated as either (1) time from birth to death for persons with a verified death certificate or (2) time from birth until end of study period (December 31, 1979).

The next phase of control selection was to create a dataset that included the names of all possible controls for each case. Matching criteria were sex, birth year (exact), cohort, and hire year (exact), plus the requirement that each potential control have a survival time equal to or greater than that of the corresponding case. From the list of all possible controls, four were selected at random by computer algorithm.

When the above criteria did not produce four or more potential controls for a case (this was true for five of the 83 cases), the criteria were relaxed sequentially as follows until four or more potential controls were found:

1. birth year $\pm$ one year, first hire exact match
2. birth year exact match, first hire $\pm$ one year
3. birth year $\pm$ one year, first hire $\pm$ one year

Once four or more potential controls were found with the relaxed criteria, four controls were randomly selected.

Four controls for four of the five cases were found by relaxing the birth year by one year (birth year $\pm$ 1) and for the fifth case by relaxing the birth year and the first hire year by one year (birth year $\pm$ 1, first hire year $\pm$ 1).

About 4,000 white workers were employed at both the facilities under study (Y-12 or ORNL). Six CNS cancer cases occurred in this group.

Controls were matched on the cohort (Y-12 or ORNL) in which the case was first employed. For two cases, matching criteria were relaxed to find four or more controls: for the first, birth and first hire years were relaxed by one year (birth year ± 1 , first year year ± 1), and for the second case, the birth year was relaxed by four years and the first hire year was relaxed by six years.

Any worker who was in a risk set for a given case based on the matching criteria could have been selected as its control. A control may have become a case later on in life. A potential control might be alive or deceased, however, but the latter must have lived at least as long as the corresponding case. A person could be a control for more than one case. In this study, four workers were controls for two cases, and one control became a case later on.

 

APPENDIX C

LUNG DOSE CALCULATION METHOD

Lung dose estimates (rem) were calculated for workers whose primary exposure was to airborne uranium compounds. A computer code was developed to consider all available data and generate individual yearly doses for use as an exposure variable in epidemiological studies. The procedure for developing lung doses was divided into two phases: (1) estimation of uranium intake and (2) calculation of the internal dose.

The intake information required for each individual included number of days worked; work area; and air concentration, chemical and physical form, and enrichment of uranium compounds present. These factors were determined from original plant documents, and data abstracted from these records were summarized to provide guides for assigning particular air monitoring data to specific work conditions. Individuals' job titles and department codes were then used to relate uranium exposure conditions to the specific individuals' work experiences.

An interactive computer program was used to input air concentration and the appropriate biological half-life for the predominant uranium compound in the area monitored. The program links these input data with an individual's work period and a number of other standard biophysical factors (lung volume, deposition fraction, S factor [Dunning et al. 1977], removal rate constant, etc.); the program then calculates dose equivalents for the year of intake and subsequent years.

Prepared by C. L. Sowder, Oak Ridge Associated Universities (ORAU); D. J. Crawford-Brown, University of North Carolina; W. G. Tankersley, ORAU; and K. Gissel, ORAU.

For example, consider a worker who is exposed to a radioactive atmosphere (or any other contaminated atmosphere) during the n year of exposure. The exposure is assumed to occur during the interval from time t_1 to time t_2 within a given year. Let the following quantities be defined during year n in the following manner:

1. C - the concentration of the radionuclide in the inhaled atmosphere (units of microcuries per cubic meter).
2. f - the fraction of the interval ($t_2 - t_1$) during which the worker was exposed to the atmosphere.
3. I - the intake rate of the contaminated atmosphere (cubic meters per day).
4. d - the deposition fraction in the organ of interest for the inhaled contaminant; here, d is the fraction of inhaled uranium deposited in the pulmonary region of the lung.
5. S - the S factor for the target organ (here the lung) and for the specific contaminant (uranium); units are rem per microcurie-day of residence in the lung.
6. λ - the removal rate constant (days^{-1}) for the contaminant from the organ; in general, λ is equal to $0.693/T$, where T is the effective halftime in the organ in units of days.
7. T - the effective halftime in the lung in units of days for uranium.

Let the interval ($t_2 - t_1$) occur at some interval within the year, that is,

Here, EOY means "End of Year" and is equal to 365 days. During the interval $(t_2 - t_1)$, the contaminant is assumed to enter the organ at a constant rate, R (microcuries per day).

The dose equivalent delivered to the organ during the year, as a result of intakes in the interval $(t_2 - t_1)$, is

$$D_{n'n} = \frac{S_n f_n I_n C_n d_n}{\lambda_n} (t_2 - t_1) - \frac{S_n f_n I_n C_n d_n}{\lambda_n^2} (1 - e^{-\lambda_n(t_2 - t_1)}) + \frac{S_n f_n I_n C_n d_n}{\lambda_n^2} (1 - e^{-\lambda_n(t_2 - t_1)}) (1 - e^{-\lambda_n(\text{EOY} - t_2)}).$$

Consider now the case of the dose equivalent delivered during this same (n) year from intakes that occurred in previous years. Assume that a previous intake occurred in year i , where i is less than n . Further assume that the intake occurred in the interval $(t_2 - t_1)$ within year i , where t_1 and t_2 are given numerical assignments relative to the first day of year i . In other words, if t_1 occurs 100 days into the year i , then t_1 is set equal to 100 days.

The total dose equivalent during year n must consider all intake intervals during year i , as well as all intake intervals in each year prior to year n . The total dose equivalent in year n from intake intervals in prior years is

$$D_{n,i} = \sum_{i=1}^{n-1} \left[\frac{S_n f_n I_n C_n d_n}{\lambda_n^2} (1 - e^{-\lambda_n(t_2 - t_1)}) e^{-\lambda_i(EOY - t_2)} \right. \\ \left. \cdot e^{-\lambda_i(n - i - 1)365(1 - e^{-365\lambda_i})} \right]$$

The total dose equivalent in year n then is the sum of the two previous equations:

$$D_n = \frac{S_n f_n I_n C_n d_n}{\lambda_n} (t_2 - t_1) - \frac{S_n f_n I_n C_n d_n}{\lambda_n^2} (1 - e^{-\lambda_n(t_2 - t_1)}) \\ + \frac{S_n f_n I_n C_n d_n}{\lambda_n^2} (1 - e^{-\lambda_n(t_2 - t_1)}) (1 - e^{-\lambda_n(EOY - t_2)}) \\ + \sum_{i=1}^{n-1} \left[\frac{S_i f_i I_i C_i d_i}{\lambda_i^2} (1 - e^{-\lambda_i(t_2 - t_1)}) e^{-\lambda_i(EOY - t_2)} \right. \\ \left. \cdot e^{-\lambda_i(n - i - 1)365(1 - e^{-365\lambda_i})} \right]$$

Once again, it must be kept in mind that t_1 and t_2 are always assigned values relative to the beginning of the year in which they occur, with this beginning always set equal to zero for each year. This means that EOY is always 365 days. Values of I must be in units of volume per day, where the volume must be in the same units as values for C .

This method results in quantitative estimates of individual lung doses and is an improvement over crude categorical exposure grouping often used in epidemiologic analyses.

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APPENDIX D

SUPPLEMENTARY TABLES FOR ALL WORKERS

TABLE D-1. DISTRIBUTION OF MATCHED SETS BY MATCHING FACTORS
(percent in parentheses)

Variable	Level	Matched Sets
Total Number of Matched Sets		89 (100.0)
Year of Birth	< 1900	9 (10.1)
	1901 - 05	15 (16.9)
	1906 - 10	13 (14.6)
	1911 - 15	14 (15.7)
	1916 - 20	18 (20.2)
	1921 - 25	11 (12.4)
	1926 - 30	7 (7.9)
	> 1930	2 (2.2)
	Mean	1913
	Median	1913
Year of First Hire	< 1945	64 (71.9)
	1946 - 50	6 (6.7)
	1951 - 55	14 (15.7)
	1956 - 60	2 (2.2)
	> 1960	3 (3.4)
	Mean	1946
	Median	1944
Age at First Hire	< 25 years	17 (19.1)
	26 - 30	17 (19.1)
	31 - 35	21 (23.6)
	36 - 40	14 (15.7)
	41 - 45	12 (13.5)
	> 45 years	8 (9.0)
	Mean	33.4 years
	Median	32.0 years

TABLE D-2. CHARACTERISTICS OF CASES (percent in parentheses)

Variable	Level	Cases
Number of Cases		89 (100.0)
Year of Death	< 1950	5 (5.6)
	1951 - 55	9 (10.1)
	1956 - 60	10 (11.2)
	1961 - 65	16 (18.0)
	1966 - 70	15 (16.9)
	1971 - 75	20 (22.5)
	> 1975	14 (15.7)
	Mean	1966
	Median	1968
Age at Death	< 40 years	11 (12.4)
	41 - 45	13 (14.6)
	46 - 50	13 (14.6)
	51 - 55	16 (18.0)
	56 - 60	12 (13.5)
	61 - 65	8 (9.0)
	> 65 years	16 (18.0)
	Mean	52.7 years
	Median	52.4 years
Tumor Type		
Brain Cancer	Glioblastoma	21 (23.6)
(ICDA8 - 191)	Astrocytoma	20 (22.5)
	Glioma	9 (10.1)
	Ependymoma	4 (4.5)
	Oligodendroglioma	2 (2.2)
	Other, specified	3 (3.4)
	Non specified	23 (25.8)
Cancers of other parts of CNS		7 (7.9)
(ICDA8 - 192)		

TABLE D-3. DISTRIBUTION OF CASES AND CONTROLS BY NONMATCHING FACTORS
(percent of cases and controls in parentheses)

Variable	Level	Cases	Controls
Number of Study Subjects		89 (100.0)	356 (100.0)
Year of Termination			
	≤ 1945	49 (55.1)	160 (44.9)
	1946 - 50	11 (12.4)	87 (24.2)
	1951 - 55	4 (4.5)	19 (5.3)
	1956 - 60	2 (2.2)	15 (4.2)
	1961 - 65	9 (10.1)	17 (4.8)
	1966 - 70	4 (4.5)	16 (4.5)
	> 1970	10 (11.2)	42 (11.8)
	Mean	1952	1951
	Median	1945	1946
Age at Termination			
	≤ 25 yrs	12 (13.5)	47 (13.2)
	26 - 30	13 (14.6)	57 (16.0)
	31 - 35	14 (15.7)	70 (19.7)
	36 - 40	10 (11.2)	44 (12.4)
	41 - 45	14 (15.7)	62 (17.4)
	46 - 50	9 (10.1)	27 (7.6)
	51 - 55	10 (11.2)	25 (7.0)
	56 - 60	4 (4.5)	7 (2.0)
	> 60 years	3 (3.4)	17 (4.8)
	Mean	38.6 years	37.6 years
	Median	38.0 years	36.0 years

TABLE D-4. SOCIOECONOMIC STATUS, ALL CASES AND CONTROLS

Distribution of Cases and Controls by Pay Code and PSU
(percent of cases and controls in parentheses)

Variable	Level	Cases	Controls
Pay Code	Hourly	77 (86.5)	295 (82.9)
	Monthly	12 (13.5)	61 (17.1)
PSU	Professional	10 (11.2)	51 (14.3)
	Skilled	73 (82.0)	259 (72.7)
	Unskilled	6 (6.7)	46 (12.9)

Matched Analyses for Socioeconomic Status

Variable	Level	Odds Ratio	95 % Confidence Interval	No. of Cases
Pay Code	Monthly	1.00	----	12
	Hourly	1.50	0.7, 3.4	77
PSU	Professional	1.00	----	10
	Skilled	1.62	0.7, 3.8	73
	Unskilled	0.73	0.2, 2.3	6
	Professional	1.00	----	10
	Skilled + Unskilled	1.47	0.63, 3.4	79
Controlling for External Radiation				
Pay Code	Monthly	1.00	----	12
	Hourly	1.40	0.6, 3.2	77
Controlling for Internal Radiation				
Pay Code	Monthly	1.00	----	12
	Hourly	1.55	0.7, 3.6	77

TABLE D-5. DURATION OF EMPLOYMENT, ALL CASES AND CONTROLS

Distribution of Cases and Controls by Duration of Employment
(percent of cases and controls in parentheses)

Level	Cases	Controls
≤ 30 days (≤ 1 month)	5 (5.6)	38 (10.7)
31 - 180 days (> 1 & ≤ 6 months)	15 (16.8)	65 (18.2)
181 - 365 days (> 6 months & ≤ 1 yr)	19 (21.3)	50 (14.0)
366 - 1095 days (> 1 yr & ≤ 3 yrs)	23 (25.8)	104 (29.2)
1096 - 3650 days (> 3 & ≤ 10 yrs)	10 (11.2)	51 (14.3)
3651 - 7300 days (> 10 & ≤ 20 yrs)	8 (9.0)	30 (8.4)
> 7300 days (> 20 yrs)	9 (10.1)	18 (5.1)
Mean	1863 days (5.1 yrs)	1467 days (4.1 yrs)
Median	447 days (1.2 yrs)	493 days (1.35 yrs)

TABLE D-5. DURATION OF EMPLOYMENT, ALL CASES AND CONTROLS (continued)

Matched Analyses for Duration of Employment

Level	Odds Ratio	95 % Confidence Interval	No. of Cases
< 1 year	1.00	----	39
> 1 & ≤ 3 yrs	0.87	0.5, 1.6	23
> 3 & ≤ 10 yrs	0.94	0.4, 2.4	10
> 10 & ≤ 20 yrs	1.36	0.4, 4.3	8
> 20 years	7.01	1.2, 41.1	9

Controlling for External Radiation

< 1 year	1.00	----	39
> 1 & ≤ 3 yrs	0.85	0.5, 1.5	23
> 3 & ≤ 10 yrs	1.12	0.4, 3.0	10
> 10 & ≤ 20 yrs	1.70	0.4, 6.7	8
> 20 years	10.80	1.25, 93.0	9

Controlling for Internal Radiation

< 1 year	1.00	----	39
> 1 & ≤ 3 yrs	0.81	0.4, 1.5	23
> 3 & ≤ 10 yrs	0.98	0.4, 2.6	10
> 10 & ≤ 20 yrs	1.35	0.4, 4.4	8
> 20 years	7.80	1.3, 46.5	9

APPENDIX E

SUPPLEMENTARY TABLES FOR WORKERS
MONITORED FOR EXTERNAL RADIATION

TABLE E-1. DISTRIBUTION OF CASES AND CONTROLS BY MATCHING FACTORS
MONITORED FOR EXTERNAL RADIATION (percent in parentheses)

Variable	Level	Cases	Controls
Number of monitored workers		27 (100.0)	90 (100.0)
Cohort	Y-12	13 (48.1)	41 (45.6)
	ORNL	9 (33.3)	35 (38.9)
	Multiple	5 (18.5)	14 (15.6)
Sex	Male	26 (96.3)	87 (96.7)
	Female	1 (3.7)	3 (3.3)
Year of Birth	< 1900	3 (11.1)	9 (10.0)
	1901 - 05	1 (3.7)	9 (10.0)
	1906 - 10	3 (11.1)	7 (7.8)
	1911 - 15	5 (18.5)	13 (14.4)
	1916 - 20	7 (25.9)	24 (26.7)
	1921 - 25	3 (11.1)	11 (12.2)
	1926 - 30	3 (11.1)	9 (10.0)
	> 1930	2 (7.4)	8 (8.9)
	Mean	1916.8	1916.7
	Median	1918	1918
Year of First Hire	< 1945	7 (25.9)	23 (25.6)
	1946 - 50	6 (22.2)	24 (26.7)
	1951 - 55	10 (37.0)	28 (31.1)
	1956 - 60	2 (7.4)	6 (6.7)
	> 1960	2 (7.4)	9 (10.0)
	Mean	1950.4	1950.5
	Median	1951	1950
Age at First Hire	< 25 yrs	2 (7.4)	8 (8.9)
	26 - 30	9 (33.3)	29 (32.2)
	31 - 35	6 (22.2)	20 (22.2)
	36 - 40	4 (14.8)	11 (12.2)
	41 - 45	3 (11.1)	12 (13.3)
	> 45 yrs	3 (11.1)	10 (11.1)
	Mean	33.6 years	33.8 years
	Median	31 years	32 years

TABLE E-2. CHARACTERISTICS OF CASES MONITORED FOR EXTERNAL RADIATION
(percent of cases in parentheses)

Variable	Level	Cases	
Number of Cases in this Group		27	(100.0)
Year of Death	≤ 1950	1	(3.7)
	1951 - 55	1	(3.7)
	1956 - 60	1	(3.7)
	1961 - 65	6	(22.2)
	1966 - 70	6	(22.2)
	1971 - 75	4	(14.8)
	> 1975	8	(29.6)
	Mean	1969	
	Median	1970	
Age at Death	≤ 40 years	3	(11.1)
	41 - 45	5	(18.5)
	46 - 50	3	(11.1)
	51 - 55	6	(22.2)
	56 - 60	4	(14.8)
	61 - 65	2	(7.4)
	> 65 years	4	(14.8)
	Mean	52.2 years	
	Median	52.4 years	
Tumor Type			
Brain Cancer	Glioblastoma	12	(44.4)
(ICDA8 - 191)	Astrocytoma	8	(29.6)
	Glioma	4	(14.8)
	Ependymoma	1	(3.7)
	Nonspecified	2	(7.4)

TABLE E-3. DISTRIBUTION OF CASES AND CONTROLS BY NONMATCHING FACTORS
MONITORED FOR EXTERNAL RADIATION (percent in parentheses)

Variable	Level	Cases	Controls
Number of Workers in this Group		27 (100.0)	90 (100.0)
Year of Termination	≤ 1945	3 (11.1)	7 (7.8)
	1946 - 50	1 (3.7)	11 (12.2)
	1951 - 55	1 (3.7)	4 (4.4)
	1956 - 60	0 (0.0)	9 (10.0)
	1961 - 65	8 (29.6)	13 (14.4)
	1966 - 70	4 (14.8)	13 (14.4)
	> 1970	10 (37.0)	33 (36.7)
	Mean	1965	1962
	Median	1968	1962
Age at Termination	≤ 25 years	1 (3.7)	1 (1.1)
	26 - 30	2 (7.4)	11 (12.2)
	31 - 35	1 (3.7)	12 (13.3)
	36 - 40	1 (3.7)	9 (10.0)
	41 - 45	4 (14.8)	14 (15.6)
	46 - 50	5 (18.5)	15 (16.7)
	51 - 55	6 (22.2)	8 (8.9)
	56 - 60	4 (14.8)	7 (7.8)
	> 60 years	3 (11.1)	13 (14.4)
	Mean	48.3 years	45.1 years
	Median	50.0 years	44.5 years

TABLE E-4. DISTRIBUTION OF SUBJECTS MONITORED FOR EXTERNAL RADIATION
BY COHORT BY CUMULATIVE EXTERNAL RADIATION DOSE
(percent of cases and of controls in parentheses)

Cohort	Level	Cases	Controls
Y-12 (after 1947)	Total	13 (100.0)	41 (100.0)
	≤ 1000 millirem	10 (77.0)	32 (78.1)
	> 1000 & ≤ 2000	2 (15.4)	3 (7.3)
	> 2000 & ≤ 3000	0 (0.0)	1 (2.4)
	> 3000 & ≤ 4000	1 (7.7)	2 (4.9)
	> 4000 & ≤ 5000	0 (0.0)	0 (0.0)
	> 5000 millirem	0 (0.0)	3 (7.3)
	Mean	947 millirem	1231 millirem
ORNL	Median	804 millirem	580 millirem
	Total	9 (100.0)	35 (100.0)
	≤ 1000 millirem	4 (44.4)	25 (71.5)
	> 1000 & ≤ 2000	4 (44.4)	2 (5.8)
	> 2000 & ≤ 3000	0 (0.0)	5 (14.3)
	> 3000 & ≤ 4000	1 (11.1)	0 (0.0)
	> 4000 & ≤ 5000	0 (0.0)	0 (0.0)
	> 5000 millirem	0 (0.0)	3 (8.6)
Multiple	Mean	1079 millirem	1372 millirem
	Median	1070 millirem	200 millirem
	Total	5 (100.0)	14 (100.0)
	≤ 1000 millirem	2 (40.0)	11 (78.6)
	> 1000 & ≤ 2000	2 (40.0)	2 (14.3)
	> 2000 & ≤ 3000	1 (20.0)	0 (0.0)
	> 3000 & ≤ 4000	0 (0.0)	0 (0.0)
	> 4000 & ≤ 5000	0 (0.0)	1 (7.1)
	> 5000 millirem	0 (0.0)	0 (0.0)
	Mean	1315 millirem	773 millirem
	Median	1690 millirem	389 millirem

TABLE E-5. SOCIOECONOMIC STATUS, MONITORED FOR EXTERNAL RADIATION

Distribution of Cases and Controls by Pay Code and PSU
(percent of cases and controls in parentheses)

Variable	Level	Cases	Controls
Pay Code	Hourly	17 (63.0)	55 (61.1)
	Monthly	10 (37.0)	35 (38.9)
PSU	Professional	9 (33.3)	30 (33.3)
	Skilled	17 (63.0)	45 (50.0)
	Unskilled	1 (3.7)	15 (16.7)

Matched Analyses for Socioeconomic Status

Variable	Level	Odds Ratio	95 % Confidence Interval		No. of Cases
Pay Code	Monthly	1.00	----		10
	Hourly	0.95	0.32,	2.85	17
PSU	Professional	1.0	----		9
	Skilled	1.06	0.36,	3.12	17
	Unskilled	0.21	0.02,	2.06	1

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TABLE E-6. DURATION OF EMPLOYMENT, MONITORED FOR EXTERNAL RADIATION

Distribution of Cases and Controls by Duration of Employment
(percent of cases and controls in parentheses)

Level	Cases	Controls
$\leq$ 1 month	0 (0.0)	2 (2.2)
> 1 month & $\leq$ 6 months	0 (0.0)	3 (3.3)
> 6 months & $\leq$ 1 year	1 (3.7)	10 (11.1)
> 1 year & $\leq$ 3 years	4 (14.8)	10 (11.1)
> 3 years & $\leq$ 10 years	6 (22.2)	22 (24.4)
> 10 years & $\leq$ 20 years	7 (25.9)	26 (28.9)
> 20 years	9 (33.3)	17 (18.9)
Mean	14.0 years	11.1 years
Median	13.1 years	9.4 years

Matched Analyses for Duration of Employment

Level	Odds Ratio	95 % Confidence Interval	No. of Cases
$\leq$ 3 years	1.00	----	5
> 3 & $\leq$ 10 years	1.38	0.27, 6.98	6
> 10 & $\leq$ 20 years	1.29	0.31, 5.40	7
> 20 years	10.95	0.94, 127.18	9

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APPENDIX F

SUPPLEMENTARY TABLES FOR WORKERS
MONITORED FOR INTERNAL RADIATION

AGE	SEX	HEIGHT	WEIGHT	DATE	TIME	LOCATION	ACTIVITY	REMARKS
20.01	87	(1.60)	70	1954	10:00	Room 101	Working	
(2.00)	81	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	85	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	85	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	81	(1.60)	70	1954	10:00	Room 101	Working	
(1.00)	81	(1.60)	70	1954	10:00	Room 101	Working	
20.01	87	(1.60)	70	1954	10:00	Room 101	Working	
(2.00)	81	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	85	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	85	(1.60)	70	1954	10:00	Room 101	Working	
(3.00)	81	(1.60)	70	1954	10:00	Room 101	Working	
(1.00)	81	(1.60)	70	1954	10:00	Room 101	Working	

TABLE F-1. DISTRIBUTION OF SUBJECTS MONITORED FOR INTERNAL RADIATION
BY MATCHING FACTORS
(percent of cases and controls in parentheses)

Variable	Level	Cases	Controls
Number of monitored workers		47 (100.0)	120 (100.0)
Cohort	Y-12 (1943-1947)	37 (78.7)	94 (78.3)
	Y-12 (After 1947)	10 (21.3)	26 (21.7)
Sex	Male	33 (70.2)	81 (67.5)
	Female	14 (29.8)	39 (32.5)
Year of Birth	< 1900	5 (10.6)	11 (9.2)
	1901 - 05	13 (27.2)	30 (25.0)
	1906 - 10	8 (17.0)	20 (16.7)
	1911 - 15	6 (12.8)	18 (15.0)
	1916 - 20	6 (12.8)	17 (14.2)
	1921 - 25	5 (10.6)	13 (10.8)
	1926 - 30	4 (8.5)	11 (9.2)
	> 1930	0 (0.0)	0 (0.0)
	Mean	1911	1912
	Median	1910	1910
Year of First Hire	< 1945	37 (78.7)	94 (78.3)
	1946 - 50	2 (4.3)	5 (4.2)
	1951 - 55	8 (17.0)	21 (17.5)
	1956 - 60	0 (0.0)	0 (0.0)
	> 1960	0 (0.0)	0 (0.0)
	Mean	1946	1946
	Median	1944	1944
Age at First Hire	< 25 years	9 (19.1)	25 (20.8)
	26 - 30	5 (10.6)	15 (12.5)
	31 - 35	11 (23.4)	29 (24.2)
	36 - 40	9 (19.1)	23 (19.2)
	41 - 45	9 (19.1)	18 (15.0)
	> 45 years	4 (8.5)	10 (8.3)
	Mean	34.4 years	33.8 years
	Median	34.0 years	34.0 years

TABLE F-2. CHARACTERISTICS OF CASES MONITORED FOR INTERNAL RADIATION
(percent of cases in parentheses)

Variable	Level	Cases
Number of Cases in this Group		47 (100.0)
Year of Death	≤ 1950	2 (4.3)
	1951 - 55	5 (10.6)
	1956 - 60	7 (14.9)
	1961 - 65	10 (21.3)
	1966 - 70	8 (17.0)
	1971 - 75	9 (19.1)
	> 1975	6 (12.8)
	Mean	1965
	Median	1965
Age at Death	≤ 40 years	5 (10.6)
	41 - 45	5 (10.6)
	46 - 50	10 (21.3)
	51 - 55	7 (14.9)
	56 - 60	4 (8.5)
	61 - 65	5 (10.6)
	> 65 years	11 (23.4)
	Mean	54.0 years
	Median	52.4 years
Tumor Type		
Brain Cancer	Glioblastoma	11 (23.4)
(ICDA8 - 191)	Astrocytoma	8 (17.0)
	Glioma	5 (10.6)
	Ependymoma	2 (4.3)
	Oligodendroglioma	2 (4.3)
	Other, specified	3 (6.4)
	Nonspecified	14 (29.8)
Cancers of other parts of CNS		2 (4.3)
(ICDA8 - 192)		

TABLE F-3. DISTRIBUTION OF SUBJECTS MONITORED FOR INTERNAL RADIATION
BY NONMATCHING FACTORS (percent in parentheses)

Variable	Level	Cases	Controls
Number of Workers in this Group		47 (100.0)	120 (100.0)
Year of Termination	< 1945	29 (61.7)	73 (60.8)
	1946 - 50	8 (17.0)	24 (20.0)
	1951 - 55	2 (4.3)	2 (1.7)
	1956 - 60	1 (2.1)	4 (3.3)
	1961 - 65	4 (8.5)	2 (1.7)
	1966 - 70	1 (2.1)	8 (6.7)
	> 1970	2 (4.3)	7 (5.8)
	Mean	1949	1950
	Median	1945	1945
Age at Termination	< 25 years	8 (17.0)	19 (15.8)
	26 - 30	3 (6.4)	11 (9.2)
	31 - 35	8 (17.0)	31 (25.8)
	36 - 40	7 (14.9)	13 (10.8)
	41 - 45	11 (23.4)	22 (18.3)
	46 - 50	4 (8.5)	10 (8.3)
	51 - 55	4 (8.5)	4 (3.3)
	56 - 60	1 (2.1)	4 (3.3)
	> 60 years	1 (2.1)	6 (5.0)
	Mean	38.0 years	37.4 years
	Median	40.0 years	35.0 years

TABLE F-4. DISTRIBUTION OF SUBJECTS MONITORED FOR INTERNAL RADIATION
BY COHORT BY CUMULATIVE LUNG DOSE (percent in parentheses)

Cohort	Level	Cases	Controls
Y-12 (1943-1947)		37 (100.0)	94 (100.0)
	≤ 15 rem	23 (62.1)	66 (70.2)
	> 15 & ≤ 30 rem	4 (10.8)	5 (5.3)
	> 30 & ≤ 45 rem	5 (13.5)	6 (6.4)
	> 45 rem	5 (13.5)	17 (18.1)
	Mean	22.0 rem	36.0 rem
	Median	5.0 rem	0.3 rem
Y-12 (After 1947)		10 (100.0)	26 (100.0)
	≤ 15 rem	9 (90.0)	22 (84.6)
	> 15 & ≤ 30 rem	1 (10.0)	1 (3.8)
	> 30 & ≤ 45 rem	0 (0.0)	0 (0.0)
	> 45 rem	0 (0.0)	3 (11.5)
	Mean	5.5 rem	11.8 rem
	Median	3.2 rem	7.0 rem

TABLE F-5. SOCIOECONOMIC STATUS, MONITORED FOR INTERNAL RADIATION

Distribution of Cases and Controls by Pay Code and PSU
(percent of cases and controls in parentheses)

Variable	Level	Cases		Controls	
Pay Code	Hourly	46	(97.9)	108	(90.0)
	Monthly	1	(2.1)	12	(10.0)
PSU	Professional	1	(2.1)	11	(9.2)
	Skilled	42	(89.4)	92	(76.7)
	Unskilled	4	(8.5)	17	(14.2)

Matched Analyses for Socioeconomic Status

Variable	Level	Odds Ratio	95 % Confidence Interval		No. of Cases
Pay Code	Monthly	1.00	---		1
	Hourly	4.13	0.51,	33.7	46
PSU	Professional	1.00	---		1
	Skilled	4.53	0.53,	38.4	42
	Unskilled	1.73	0.17,	17.8	4

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TABLE F-6. DURATION OF EMPLOYMENT, MONITORED FOR INTERNAL RADIATION

Distribution of Cases and Controls by Duration of Employment
(percent of cases and controls in parentheses)

Level	Cases	Controls
$\leq$ 1 month	1 (2.1)	14 (11.7)
> 1 month & $\leq$ 6 months	11 (23.4)	33 (27.5)
> 6 months & $\leq$ 1 year	10 (21.3)	25 (20.8)
> 1 year & $\leq$ 3 years	14 (29.8)	22 (18.3)
> 3 years & $\leq$ 10 years	7 (14.9)	13 (10.8)
> 10 years & $\leq$ 20 years	2 (4.3)	7 (5.8)
> 20 years	2 (4.3)	6 (5.0)
Mean	3.46 years	3.47 years
Median	1.1 years	0.8 year

Matched Analyses for Duration of Employment

Level	Odds Ratio	95 % Confidence Interval	No. of Cases
$\leq$ 1 year	1.00	---	22
> 1 & $\leq$ 3	2.10	0.88, 5.0	14
> 3 & $\leq$ 10	1.80	0.33, 9.8	7
> 10 years	0.75	0.05, 11.0	4

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